Answer 1:

Bibliographic Information

Inhibition of Shc/Grb2 protein-protein interaction suppresses growth of B104-1-1 tumors xenografted in nude mice. Kim, Hyae-Kyeong; Jeong, Moon-Jin; Kong, Mi-Young; Han, Mi Young; Son, Kwang-Hee; Kim, Hwan Mook; Hong, Su Hyung; Kwon, Byoung-Mog. Korea Research Institute of Bioscience and Biotechnology, Taejon, S. Korea. Life Sciences (2005), 78(3), 321-328. Publisher: Elsevier B.V., CODEN: LIFSAK ISSN: 0024-3205. Journal written in English. CAN 144:16577 AN 2005:1173418 CAPLUS

Abstract

Actinomycin D was revealed as an inhibitor of Shc/Grb2 interaction in cell lines from our recent study. Shc and Grb2 proteins are important mols. in Ras signaling pathways leading to cellular differentiation and proliferation, which require dramatic morphol. changes. It was detected by transmission electron microscopy that actinomycin D induced significant changes in cellular ultrastructures of B104-1-1 cells and confirmed that the changes were due to inhibition of Shc/Grb2 interaction by actinomycin D rather than its inhibitory effect on transcription. Because actinomycin D was dispersed mainly in cytoplasm and Shc peptide (synthetic 13 amino acid tyrosine phosphorylated polypeptide) successfully displaced actinomycin D binding to its cellular targets while the other polypeptide from PDGF receptor could not. We examd. the effect of actinomycin D on growth of B104-1-1 tumor xenografted in nude mice. Tumor growth was inhibited in vivo after treatment with this inhibitor. Efficacy was correlated with a redn. in the levels of Shc/Grb2 binding in excised tumors. These results suggest that actinomycin D inhibited Shc/Grb2 interaction in B104-1-1 tumor xenografted in nude mice.

Answer 2:

Bibliographic Information

The synthesis, discovery, and development of a highly promising class of microtubule stabilization agents: curative effects of desoxyepothilones B and F against human tumor xenografts in nude mice. Chou, Ting-Chao; O'Connor, Owen A.; Tong, William P.; Guan, Yongbiao; Zhang, Zui-Guo; Stachel, Shawn J.; Lee, Chulbom; Danishefsky, Samuel J. Preclinical Pharmacology Core Facility, Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Proceedings of the National Academy of Sciences of the United States of America (2001), 98(14), 8113-8118. Publisher: National Academy of Sciences, CODEN: PNASA6 ISSN: 0027-8424. Journal written in English. CAN 135:327022 AN 2001:526491 CAPLUS

Abstract

We have evaluated two synthetic epothilone analogs lacking the 12,13-epoxide functionality, 12,13-desoxyepothilone B (dEpoB), and 12,13-desoxyepothilone F (dEpoF). The concns. required for 50% growth inhibition (IC50) for a variety of anticancer agents were measured in CCRF-CEM/VBL1000 cells (2,048-fold resistance to vinblastine). By using dEpoB, dEpoF, aza-EpoB, and paclitaxel, the IC50 values were 0.029, 0.092, 2.99, and 5.17 μM, resp. These values represent 4-, 33.5-, 1,423- and 3,133-fold resistance, resp., when compared with the corresponding IC50 in the parent [nonmultiple drug-resistant (MDR)] CCRF-CEM cells. We then produced MDR human lung carcinoma A549 cells by continuous exposure of the tumor cells to sublethal concns. of dEpoB (1.8 yr), vinblastine (1.2 yr), and paclitaxel (1.8 yr). This continued exposure led to the development of 2.1-, 4,848-, and 2,553-fold resistance to each drug, resp. The therapeutic effect of dEpoB and paclitaxel was also compared in vivo in a mouse model by using various tumor xenografts. DEpoB is much more effective in reducing tumor sizes in all MDR tumors tested. Anal. of dEpoF, an analog possessing greater aq. soly. than dEpoB, showed curative effects similar to dEpoB against K562, CCRF-CEM, and MX-1 xenografts. These results indicate that dEpoB and dEpoF are efficacious antitumor agents with both a broad chemotherapeutic spectrum and wide safety margins.

Answer 3:

Bibliographic Information

Development of human lymphoma/leukemia xenograft models in immune-deficient mice for evaluation of potential anticancer agents. Dykes, D. J.; Hollingshead, M. G.; Camalier, R. F.; Waud, W. R.; Mayo, J. G. Southern Research Institute, Birmingham, AL, USA. Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 295-304. Publisher: S. Karger AG, CODEN: COONEV ISSN: 0250-3220. Journal written in English. CAN 133:217399 AN 2000:242563 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eleven human lymphoma/leukemia cell lines were assessed as in vivo xenograft models in severe combined immunodeficient (SCID) mice. In prepn. for efficacy evaluations of new antitumor agents, all eleven cell lines have been characterized for sensitivity to known clin. useful agents. The lines included in the study represent a variety of diseases including T-cell, myelogenous, and lymphoblastic leukemias, as well as histiocytic, B-cell and Burkitt's lymphomas. The selected agents for this study were representative of various chem. classes. Addnl., growth studies were performed including comparisons in athymic nude mice. These studies were designed to det. s.c. tumor vol. doubling times, graft success, latent growth periods, and other characteristics necessary to effectively implement and interpret anticancer efficacy evaluations. The various tumor lines used proved to be good models for chemotherapy trials. In the chemotherapy trials, considerable independent chemotherapeutic profiles were obsd. but there were also some similarities among the various histol. types.

Answer 4:

Bibliographic Information

Cytokine messenger RNA stability is enhanced in tumor cells. Ross, Helen J.; Sato, Noriharu; Ueyama, Yoshito; Koeffler, H. Phillip. Dep. Med., UCLA, Los Angeles, CA, USA. Blood (1991), 77(8), 1787-95. CODEN: BLOOAW ISSN: 0006-4971. Journal written in English. CAN 114:245716 AN 1991:245716 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Hematopoietic growth factors are produced by a no. of human tumors. RNA was extd. from selected human tumor cells known to produce at least one hematopoietic growth factor and high levels of abnormally stable cytokine mRNA were found. Half-line expts. performed after preventing RNA synthesis by exposing cells to actinomycin D before RNA extn. showed stabilization of cytokine messages in tumor cells in liq. culture as well as in human tumor xenografts grown in mice. Exposure to the phorbol ester phorbol 12-myristate 13-acetate (TPA) caused enhancement of granulocyte-macrophage colony-stimulating factor (GM-CSF) message level in lung cancer cells and in control fibroblasts but elevated levels persisted far longer in the tumor cells. In normal cells, an AU-rich sequence in the 3' untranslated region of cytokine mRNAs confers lability to the message. Although a β-globin gene expression vector contg. this region appears to produce unstable mRNA in lung cancer cells, cytokine mRNAs, which also contain this sequence, are very stable in the tumors studied. This may indicate that another region of the cytokine mRNA mol. is of greater importance than the AU-rich region in detg. stability in tumor cells.

Answer 5:

Bibliographic Information

Development of drug resistance in a human epidermoid lung carcinoma xenograft line. Mattern, J.; Bak, M., Jr.; Hoever, K. H.; Volm, M. Inst. Exp. Pathol., Cancer Res. Cent., Heidelberg, Fed. Rep. Ger. British Journal of Cancer (1988), 58(1), 30-3. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 109:183130 AN 1988:583130 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The development of resistance to vincristine, actinomycin D, and cisplatin has been examd. in a human epidermoid lung carcinoma

xenograft line (HXL 55) growing in nude mice. Treatment of HXL 55 with 1 mg/kg vincristine or 0.5 mg/kg actinomycin D once in each in vivo passage resulted in a rapid redn. in tumor responsiveness to these drugs. A partial resistance was already acquired at the 2nd transplant generation. In contrast, a gradual decrease in therapeutic response was obsd. with 10 mg/kg cisplatin. Irradn. with a local dose of 10 Gy induced no resistance. The three induced drug-resistant sublines were characterized in terms of the time course of development of resistance, the degree of induced resistance cross-resistance, growth rate, and stability of the phenotype.

Answer 6:

Bibliographic Information

New actinomycin D analogs as superior chemotherapeutic agents against primary and advanced colon tumors and colon xenografts in nude mice. Sengupta, Sisir K.; Kogan, Yuri; Kelly, Christine; Szabo, Josephine. Sch. Med., Boston Univ., Boston, MA, USA. Journal of Medicinal Chemistry (1988), 31(4), 768-74. CODEN: JMCMAR ISSN: 0022-2623. Journal written in English. CAN 108:142951 AN 1988:142951 CAPLUS

Abstract

"Reverse" analogs (RAD's) of actinomycin D (AMD) and their antitumor activity against mouse and human colon tumor cells are reported. RAD's are tetracyclic, and they have an oxazole ring fused on the tricyclic phenoxazine chromophore of AMD (I-III). In tumor cells and rat hepatic microsomes, RAD's are metabolized to a tricycli "sym." analog of AMD (SAD; IV) with the loss of the oxazole ring and its substituents. RAD and SAD are very active in priming superoxides in the presence of microsomal enzymes as well as in inhibiting the synthesis of DNA and the growth of human colon tumor HT-29 cells in vitro. III, the prepn. of which is described, and SAD efficiently cleave closed circular plasmid pBR322 DNA, like the antitumor agent bleomycin. In addn. to their strong inhibitory activity against P388 and B16 tumor in vitro and in vivo, III and SAD demonstrate high levels of activity against primary C26 and advanced C38 colon tumors in mice and against a xenograft of human colon adenocarcinoma CX-1 in athymic mice. In all these biol. activities, the analogs demonstrate superiority to AMD (V) in several exptl. tumors. Also, the analogs, in contrast to AMD, show reduced toxicity in tumor-free mice, which is possibly due to the metabolic deactivation of SAD in host organs.

Answer 7:

Bibliographic Information

Altered cell morphology and transplantability of the mouse tumor with acquired resistance to actinomycin D and 5-fluorouracil. Fujimoto, J.; Mori, T. Fac. Med., Osaka Univ., Osaka, Japan. Editor(s): Ishigami, Joji. Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th (1985), Anticancer Sect. 1 211-12. Publisher: Univ. Tokyo Press, Tokyo, Japan CODEN: 55GNAX Conference written in English. CAN 105:202840 AN 1986:602840 CAPLUS

Abstract

C3H mouse Fujimoto ascites tumor cells (FAT), with acquired resistance to actinomycin D [50-76-0] (FAT-AD), exhibited a redn. in xenotransplantability. However, FAT cells treated with 5-fluorouracil [51-21-8] (FAT-FU) showed neither considerable resistance to the drug nor reduced xenotransplantability. FAT-AD cells had a smaller diam., and fewer and shorter microvilli on their surface than parental FAT cells. The diam. and microvilli of FAT-FU cells were similar to those of FAT cells. Not only was the amt. of trypsin-releaseable membrane glycopeptides (MGP) of FAT-AD or FAT-FU cells lower but the sugar contents of these peptides were lower than in FAT cells. The sugar-rich fraction of MGP from each ascites subline contained glycopeptides of mol. wt. 105,000; this mol. is made up of 2 units, each of mol. wt. 56,000.

Answer 8:

Bibliographic Information

Chemotherapy of human yolk sac tumor heterotransplanted in nude mice. Sawada, Masumi; Matsui, Yoshiaki; Okudaira, Yoshio. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. JNCI, Journal of the National Cancer Institute (1983), 71(6), 1221-5. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 100:96258 AN 1984:96258 CAPLUS

Abstract

The chemotherapeutic effects of cis-diamminedichloroplatinum [15663-27-1] plus vinblastine [865-21-4] plus bleomycin [11056-06-7] (PVB) on 3 human yolk sac tumors (YST-1, YST-2, and YST-3) of the ovary, which were heterotransplanted into BALB/c nude mice, were compared with the effects of vincristine+actinomycin D+cyclophosphamide (VAC), the combination currently favored for treatment of yolk sac tumors. Both PVB and VAC significantly reduced the tumor vol. of all the treated tumors. The mean wts. of tumors in animals treated with PVB or VAC were, in percent of the mean tumor wt. in untreated animals: 1.3 and 1.6 for YST-1, 2.5 and 3.3 for YST-2, and 5.5 and 2.7 for YST-3, resp. A strong correlation was noted between tumor vol. and α-fetoprotein level in the sera of mice bearing YST-1 or TST-2 tumors.

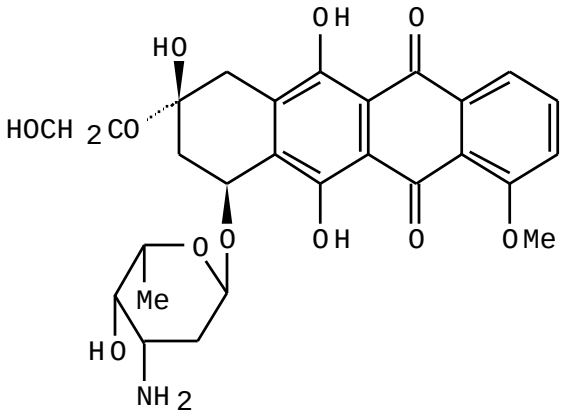
Answer 9:

Bibliographic Information

Chemotherapeutic response in xenografts: inter- and intra-tumor heterogeneity. Houghton, Peter J.; Houghton, Janet A. Dep. Biochem. Clin. Pharmacol., St. Jude Children's Res. Hosp., Memphis, TN, USA. UCLA Symposia on Molecular and Cellular Biology, New Series (1983), 4(Ration. Basis Chemother.), 61-9. CODEN: USMBD6 ISSN: 0735-9543. Journal written in English. CAN 98:209649 AN 1983:209649 CAPLUS

Abstract

The sensitivity of 5 lines of rhabdomyosarcoma, each derived from a different child and grown as xenografts in mice, was examd. to doxorubicin (I) [23214-92-8] actinomycin D (II) [50-76-0] and vincristine (III) [57-22-7]. Resistance de novo to 1 agent was not assocd. necessarily with cross resistance. Development of resistance to vincristine in situ was examd. Resistant lines were derived only from 2 tumor lines which showed a slight sensitivity to vincristine initially. Apparently, the initial tumor response is detd. by subpopulations of cells having different intrinsic sensitivity to vincristine.



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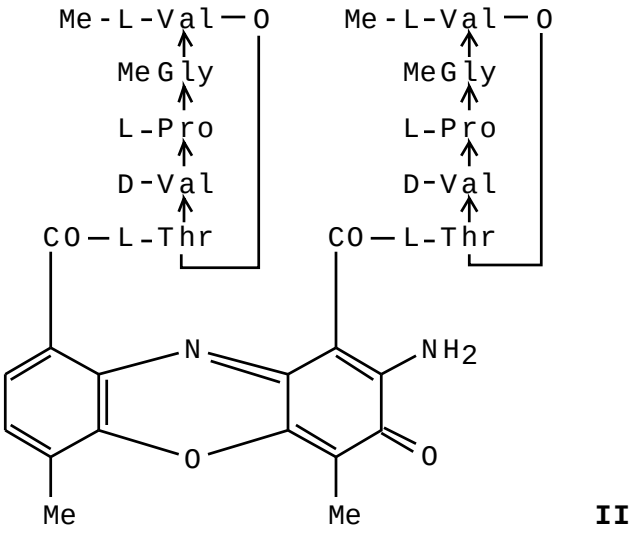
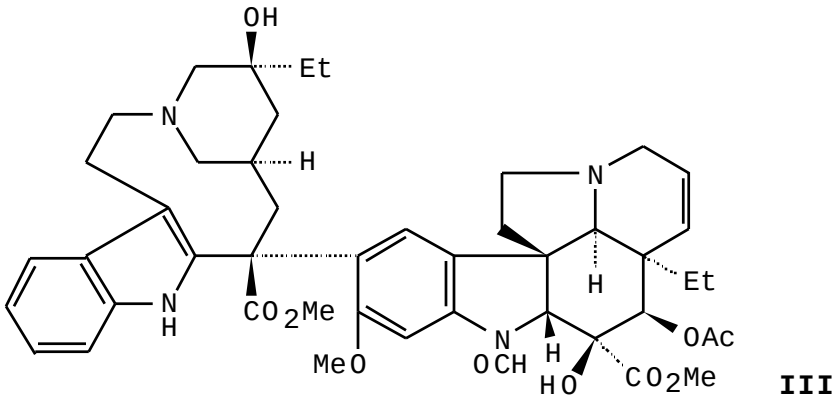


II



III

Answer 10:

Bibliographic Information

Use of heterotransplants in diffusion chambers for determining the individual drug sensitivity of human ovarian cancer to chemotherapeutic drugs. Sobol, I. L.; Marenich, A. F. Cancer Res. Cent., Moscow, USSR. Byulleten Eksperimental'noi Biologii i Meditsiny (1979), 88(8), 243-5. CODEN: BEBMAE ISSN: 0365-9615. Journal written in Russian. CAN 91:150972 AN 1979:550972 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The sensitivity of 10 ovarian tumor heterotransplants in diffusion chambers in mice to hexamethylmelamine [645-05-6], cyclophosphane [50-18-0], 5-fluorouracil [51-21-8], methotrexate [59-05-2], dactinomycin [50-76-0], 17-hydroxyprogesterone caproate [630-56-8], and thiotepa [52-24-4] was variable. E.g., hexamethylmelamine, cyclophosphane, 5-fluorouracil, and methotrexate had a brief inhibiting effect in growth of a solid glandular cancer, inhibited growth of a glandular papillary cancer, and had no effect on growth of a papillary adenocarcinoma. In 4 of 5 cases where results of these expts. were compared with results of expts. obtained in the treatment of patients with the same drugs, exptl. results correlated with clin. findings.